

# Subject Index

- A**cute lymphoblastic leukemia (ALL),  
     IL-6 production in, 391-394  
 Acute myelogenous leukemia (AML),  
     294-299  
 Acute phase proteins (APP). *See also*  $\alpha_1$  acid  
     Glycoprotein; C-reactive protein;  
     Serum amyloid A  
     in endometriosis, 508-509  
     genes of, 16  
     glycosylation of  
       changes in, 319-322  
       cytokine regulation of, 323-325  
       IL-6-type cytokines and, 413-415  
       mechanism of, 325-327  
       pathophysiological changes, 322-323  
     induction of  
       by cytokines, 15-16  
       by IL-6, 313-315, 419-421  
       by OSM, 47-48  
       post-transcriptional mechanisms in,  
       102-106  
     in ischemia, 493-495  
     in NBL, 443-444  
     synthesis of, 419-421  
 Acute phase response (APR)  
     cytokines involved in, 2, 108-109  
     hormonal modification of, 108  
     in IL-6-deficient mice, 377  
     LPS induction of, 108, 111-112,  
     114-115  
     modified proteins in, 108-115  
     after surgery, 505-507  
     turpentine-induced, 377-379  
 Acute phase response elements (APREs)  
     in APP genes, 16  
     DNA binding factors and, 58-59  
     in IL-6 signal pathway, 57  
     JEBS binding of, 60-62  
     NF-IL6 binding to, 17  
     Stat protein recognition of, 58-59  
 Acute phase response factors (APRFs)  
     activation of, 226-230, 377-379  
     JEBS binding to, 60-62  
     molecular cloning of, 20-23  
     tyrosine phosphorylation of, 23-24,  
     229-231  
 Adenovirus vectors  
     biological activity of, 286-290  
     construction of, 284-285  
     for cytokine gene expression, 282-283  
 Adrenocorticotrophic hormone (ACTH),  
     IL-1/IL-6 and, 71, 79  
 AIDS  
     anti-IL-6 therapy, 131  
     IL-6 levels in, 130  
 ALL. *See* Acute lymphoblastic leukemia  
 All-trans retinoic acid (ATRA), 457-458  
 Alzheimer's disease, IL-6 levels in, 130  
 AML. *See* Acute myelogenous leukemia  
 Antioxidants  
     and inflammatory cytokine production,  
     332-338  
     molecular biological effects of, 336-338  
 Aplasia, IL-6 levels in, 439  
 APREs. *See* Acute phase response elements  
 APRFs. *See* Acute phase response factors  
 Asthma. *See also* Respiratory inflammation  
     IL-6-type cytokines and, 89  
     IL-11 in, 89-90  
     respiratory viruses and, 97  
 ATRA. *See* All-trans retinoic acid  
**B**acterial endotoxin (LPS)  
     APR induction by, 108  
     IL-1/IL-6 induction by, 111-114, 222  
     and inflammatory cytokine production,  
     332-338  
     *op/op* mouse resistance to, 499-501  
     and septic shock, 315, 336-338  
 BAL. *See* Bronchoalveolar lavage  
 BMT. *See* Bone marrow transplantation  
 Bone marrow transplantation (BMT), and  
     CRP/IL-6 levels, 440-441  
 Bronchoalveolar lavage (BAL)  
     and asthma, 89  
     IL-6 levels in, 287-290, 455-456  
**C**achexia  
     IL-6 levels in, 130-131  
     OSM and, 43  
 Cancer. *See also* specific cancers  
     asbestos-related  
       CRP levels and, 435-437  
       IgE levels and, 435-436  
     IL-6 and, 385-387  
     IL-6 serum levels in, 130, 446-448  
     and post-surgical HMW Fb increase,  
     388-390  
 Cardiotrophin-1 (CT-1). *See also* IL-6-type  
     cytokines  
     and cardiac myocyte hypertrophy, 12  
     and gp130, 1-2  
 C/EBP  
     expression of, 19  
     family members, 16, 19  
     and IL-6 promoter induction, 2-3  
     p53 and, 4-10  
     tyrosine kinase activation of, 262

- C/EBP $\beta$ -deficient mice  
 APR in, 269–270, 377  
 lymphoproliferative alterations in, 270–272
- Chronic arterial occlusion. *See* Ischemia
- Ciliary neurotrophic factor (CNTF). *See also* Inflammatory cytokines;  
 Interleukin-6-type cytokines  
 in APP induction, 15  
 in APRF phosphorylation, 23–24  
 in C/EBP family, 19  
 cytokines related to, 37  
 and gp130, 1–2  
 in septic shock, 407–409
- Ciliary neurotrophic factor (CNTF) receptor, 213–215
- CNTF. *See* Ciliary neurotrophic factor
- Corticosteroid receptors. *See* Glucocorticoid receptors
- C-reactive protein (CRP)  
 as APP, 109  
 in chronic arterial occlusion, 493–495  
 IL-6 induction of, 102–104, 106  
 mRNA half life, 105  
 in neonatal infection diagnosis, 398–399  
 regulation of, 103–106  
 serum levels of  
   and asbestos-related cancer, 435–437  
   after BMT, 440–441  
   IL-6 and, 435–436  
   after surgery, 505–507
- CRP. *See* C-reactive protein
- CRU. *See* Cytokine response unit
- CSF-1. *See* Macrophage growth factor
- CT-1. *See* Cardiotrophin-1
- Cytokine receptors. *See also* Hematopoietin receptors  
 SIF activation and, 196–203
- Cytokine response unit (CRU)  
 binding factor (YY1), 239, 241–242  
 NF $\kappa$ B competition with, 245–249  
 in SAA1-promoter repression, 242–245  
 binding sites within, 239
- Cytokines. *See also* Inflammatory cytokines;  
 Interleukin-6-type cytokines  
 and APP induction, 15–16  
 and corticosteroid receptors, 71–76  
 glucocorticosteroid inhibition of, 79–80  
 using gp130, 1–2  
 IL-6-type, 1–2  
 in IL-11 regulation, 92  
 induction of  
   by LPS, 111–112  
   by taxol, 112, 114  
 in ISGF3 activation, 24–25  
 and liver cell metabolism, 416–418  
 in mammalian development regulation, 29  
 networks of, 71, 76  
   and GCSB, 73–75  
   and glucocorticosteroid production, 71  
   and SOD activity, 416–418  
   synthesis/release of, 109, 111–115  
   and TAT activity, 416–418
- D**-factor. *See* Differentiation stimulating D-factor
- Differentiation stimulating (D)-factor/LIF receptor, 480–481
- Disease, IL-6 role in, 130–131
- DNA-binding factors, IL-6-induced, 58–59
- E**2. *See* Estradiol
- Endometriosis  
 APP in, 508–509  
 inflammatory cytokine levels in, 496–498
- 17 $\beta$ -Estradiol (E2), and IL-6 gene expression, 82–84
- Ets binding site (JEBS)  
 APRF binding with, 60–62  
 in IL-6 signal transduction, 57–58  
 in JRE-IL6, 55
- G**AS. *See*  $\gamma$ -Interferon activated site
- GCSB. *See* Glucocorticosteroid binding
- Glucocorticoid receptors (GR)  
 cytokine networks and, 71–76  
 and gene expression, 80–81  
 and NF- $\kappa$ B, 81, 84  
 p65 and, 82  
 and transcription factors, 80  
 in transcription factor superfamily, 79
- Glucocorticoid response elements (GRE), 80
- Glucocorticoids  
 and cytokine blood levels, 71  
 and IL-6 gene expression, 80–81  
 immune system actions of, 79–80
- Glucocorticosteroid binding (GCSB)  
 basal level of, 73–75  
 inflammatory cytokines and, 71, 73–76
- $\alpha$ 1 acid Glycoprotein (AGP)  
 in chronic arterial occlusion, 493–495  
 IL-6 REs and, 16  
 induction of, 422  
 regulation of, 252
- gp80. *See also* Interleukin-6 receptor  
 cytokine regulation of, 465–467
- gp130. *See also* Interleukin-6 receptor;  
 Interleukin-6-type cytokines;  
 Soluble gp130  
 cytokine regulation of, 465–467  
 functional epitopes on, 482–484  
 and IL-6R endocytosis, 410–412  
 in IL-11 receptor, 2  
 in *jumB* activation, 56–57  
 phosphorylation of, 23–24, 231–232

- signal transducer function of, 55  
signal transduction through, 25-26  
GR. *See* Glucocorticoid receptor
- H**  
H7-sensitive kinases. *See also* Protein kinases  
in IL-11 signaling, 33, 37  
H7-sensitive pathway  
in IL-6 RE activation, 62-64  
in IL-6 signal transduction pathway, 56  
in *junB* activation, 56-57  
in signal transduction, 55-57  
Hematopoietin receptors. *See also* Cytokine receptors  
APP gene regulation by, 191-194  
ligands for, 166-169  
and SIF activation, 196-203  
subunits of  
functions of, 189-190  
signaling function of, 194-196  
Hepatic acute phase gene classes, 252-253  
Hepatocyte growth factor (HGF)  
and APP synthesis, 419-421  
and TAT/SOD activity, 416-418  
hFDGI. *See* Human fibroblast-derived growth inhibitor  
HGF. *See* Hepatocyte growth factor  
High molecular weight fibrinogen (HMW Fb), post-operative levels of, 388-390  
Histamine, 92-93, 96  
HMW Fb. *See* High molecular weight fibrinogen  
Human fibroblast-derived growth inhibitor (hFDGI), IL-6 identity of, 1
- I**  
Immunoglobulin E (IgE)  
post-surgical response of, 477-479  
serum levels of  
and asbestos-related cancer, 435-437  
IL-4 and, 435-436  
Inflammatory cytokines. *See also* Ciliary neurotrophic factor; Interleukins; Leukemia inhibitory factor; Oncostatin M; Tumor necrosis factor  
antioxidants and, 332-338  
in endometriosis, 496-498  
inhibition of, 331  
 $\gamma$ -Interferon activated site (GAS). *See also* Palindromic interferon response element  
IL-6RE binding to, 58  
Stat factor binding to, 56  
Interferon- $\alpha$  (IFN- $\alpha$ )  
and adrenal cortex regeneration, 491-492  
and myeloma cell growth, 457-458  
Interferon-stimulated gene factor 3 (ISGF3), 16, 24-25  
Interleukin-1 (IL-1)  
and ACTH levels, 71, 79  
in AGP induction, 252  
antioxidants and, 331-338  
in APP induction, 15, 102-106  
synthesis/release of, 109, 111-115  
Interleukin-1 $\beta$  (IL-1 $\beta$ )  
and GCSB, 71, 73-76  
in SAA induction, 102-105  
TIMP-1 induction by, 462-464  
Interleukin-6 (IL-6)  
and ACTH levels, 71, 79  
action mechanism of IL-6, 129-130  
activity of, 55  
AGP regulation by, 252  
in ALL, 391-394  
APP induction by, 15, 102-106  
and APP synthesis  
HGF and RA influence on, 419-421  
after tissue damage/infection, 313-315  
and APR, 1-2  
in APRF phosphorylation, 23-24, 229-231  
in B cell differentiation, 311-313  
biological activities of, 129  
and cancer, 385-387  
clinical applications of, 380-383  
in CNS, 403-405  
in CRP induction, 102-105, 252  
cytokines related to, 37, 213-215, 222  
and cytotoxic chemotherapy  
clinical trials with, 357  
evaluation of, 359-360  
effect on leukemic cell lines, 294-296  
functional analysis of, 262-263  
C/EBP $\beta$ -deficient mice in, 269-272  
by gene targeting, 265-272  
IL-6-deficient mice in, 265-269  
and GCSB, 71, 73-76  
hFDGI identified as, 1  
and human myeloma cells, 132  
and IgE response, 477-479  
IL-6 mutant antagonists of, 131-132  
and IL-6R, 222-223  
induction of  
by CRP, 109  
by LPS, 111, 266  
by taxol, 112, 114  
IRF-1 gene pIRE enhancer activation by, 349-352  
*junB* gene induction by, 56-57  
kinase activation by, 55-56. *See also* Tyrosine kinases  
and leukemic blast cell growth, 295-296  
and leukemic cell lines, 294-295  
and LPS-induced septic shock, 315

- and MDS, 299-300
  - mechanism of action of, 129-130
  - mRNA expression
    - in CNS, 403-405
    - lesion-induced, 488-490
  - multiple effects of, 55
  - murine-human chimeras, 422-423
  - in myeloid leukemic cell line M1,
    - 485-486
  - myeloproliferative disease models,
    - 301-302
  - in neonatal infection diagnosis, 398-399
  - and *N-ras* genes activation, 300
  - OSM induction of, 48
  - and osteoclast activation, 377
  - in osteoporosis, 212, 376-377
  - physiologic actions of, 282
  - production of
    - in ALL, 391-394
    - antioxidants and, 332-335
    - cell types involved in, 120, 308
    - inhibition of, 331-332, 338
  - in PTL, 10-12
  - receptor-binding residues of, 400-402
  - regulatory actions of, 55
  - response modulation, 4-10
  - role in disease, 130-131
  - in SAA induction, 104-105
  - serum levels of
    - in AIDS, 130-131
    - in aplasia, 439
    - in BAL, 455-456
    - after BMT, 440-441
    - in cutaneous disease, 432-433
    - diagnostic/prognostic value of, 10-12
    - diurnal variations in, 468-470
    - fluoxetine treatment and, 474-475
    - in ischemia, 493-495
    - in ovarian cancer, 446-448
    - post-operative, 506-507
    - in septic shock, 407-409
  - signal transduction residues of, 400-402
  - structure-function analysis of, 131
  - synthesis/release of, 109, 111-115
  - TIMP-1 induction by, 462-464
  - tyrosine kinase activation by, 55
- Interleukin-6 (IL-6) action
- on murine tumor models
    - mechanisms of, 346-352
    - metastasing tumor models, 343-346
    - myeloid leukemia models, 342-343
  - on transcription factor regulation,
    - 347-349
  - on tumor cells
    - immune system involvement in,
      - 346-347
    - IRF-1/IRF-2 and, 347-348
- Interleukin-6 (IL-6) chaperones
- antibodies as, 123-125
  - in blood, 120-121
  - and IL-6 masking, 121-123
  - and immunotherapy-induced IL-6 levels,
    - 125-126
- Interleukin-6 (IL-6)-deficient mice. *See also op/op* mice
- APP synthesis in, 313-315
  - B cell differentiation in, 311-313
  - bone defects in, 267-268
  - CFU-s reduction in, 309-310
  - embryonic development of, 309
  - generation of, 265-267, 309
  - inflammatory response in, 268-269
  - osteoclast activity in, 375-377
  - osteoporosis in, 375-377
  - ovariectomy-induced bone loss in,
    - 375-377
  - pleiotropic defects in, 308-309
  - septic shock protection in, 315
  - T cell growth/function in, 310-311
- Interleukin-6 (IL-6) gene expression
- adenovirus vectors for, 282-290
  - E2 regulation of, 82-84
  - glucocorticoid repression of, 80-81
  - and *N-ras* gene activation, 300
  - steroid regulation of, 79-80
- Interleukin-6 (IL-6) promoter
- p53 and, 5-7
  - transcription factors and, 2-3
- Interleukin-6/LIF response factor, 502-503
- Interleukin-6-like immunoreactivity, 450-451
- Interleukin-6 receptor (IL-6R). *See also* Interleukin-6-type cytokine receptors; Soluble Interleukin-6 receptor
- gp80 subunit of, 55, 465-467
  - gp130 subunit of, 2, 55, 465-467
  - high-affinity-complex stoichiometry,
    - 471-473
  - IL-6/IL-6R internalization, 223-224
  - models of interaction of, 130
  - mRNA expression, in CNS, 403-405
  - and myeloma cell growth, 457-458
  - signal mediation by, 64-67
  - signal transduction through, 55-56. *See also* IL-6 signal transduction pathway
  - soluble subunits of, 64-67
- Interleukin-6 receptor (IL-6R) antagonists, 129
- development/characterization of, 131
  - and IL-6 activity on myeloma cells,
    - 132-133

- molecular design of, 136-137, 147-149, 215-218
  - IL-6 mutagenesis, 139, 142-147
  - and IL-6R $\alpha$ /gp130 interface, 144-147
  - molecular modeling, 138-141
  - superantagonist generation, 143-144
- Interleukin-6 response elements (IL-6 RE)
  - activation of, 56, 62-64
  - in APP genes, 16
  - DNA motifs in, 55
  - GAS affinity for, 58
  - IL-6-induced DNA binding factors and, 58-59
- JEBS-APRF binding, 60-62
- JRE-IL6, 55
- proteins binding with, 252-253, 256-258
  - amino acid sequence analysis of, 255-256
  - purification of, 253-255
- Stat protein binding to, 62, 459-461
- tyrosine phosphorylation and, 62
- Interleukin-6 signal transduction pathway
  - APRE activation by, 56, 62-64
  - and gp130 phosphorylation, 231-233
  - H7-sensitive pathway in, 56, 62-64
  - IL-6R and, 55-56
  - IL-6 RE activation by, 62-64
  - JEBS factors mediation of, 57-58
  - model of, 233
  - protein kinases and, 55-56
  - Stat protein involvement in, 55-56, 58-59
- Interleukin-6-type cytokine receptors. *See also* Hematopoietin receptors
  - APP gene elements regulation by, 191-194
- Interleukin-6-type cytokines. *See also* Cardiotrophin-1; Ciliary neurotrophic factor; Interleukin-11; Leukemia inhibitory factor; Oncostatin M
  - and AML, 297-299
  - and APP glycosylation, 319-326, 413-415
  - clinical applications of, 383-385
  - and CRP levels, 435-437
  - in gene therapy of melanoma, 361-371
  - and glycosylation regulation, 323-325
  - and gp130, 1-2, 23-24, 42
  - and IgE levels, 435-437
  - and leukemic cell lines, 294-295
  - and melanoma, 369-371
  - and myeloproliferative disease models, 301-303
  - soluble receptor subunits of, 213-215
  - and TAT/SOD activity, 416-418
- Interleukin-8 (IL-8), and selectin-P-mediated platelet adhesion, 395-397
- Interleukin-11 (IL-11)
  - in airway fluids, 94-95
  - and airways hyperresponsiveness, 95-96
  - in APP induction, 15
  - in asthma, 89-90
  - biologically active regions of, 152-153, 160-163
  - clinical applications of, 384-385
  - cytokine regulation of, 92
  - cytokines related to, 37
  - and gp130, 1-2, 37
  - histamine regulation of, 92-93
  - infectious agent stimulation of, 93-95
  - kinase activation by, 31-37
  - and leukemic blast cell growth, 297
  - and leukemic cell lines, 295, 297
  - lung cell production of, 91-92
  - mutagenesis of
    - and biological activity, 159-163
    - C-terminal alanine-scan, 155-158, 161-163
    - N-terminal alanine-scan, 158-163
  - myeloproliferative disease models, 301-302
  - pleiotropic nature of, 90
  - primary response gene activation by, 36-37
  - in pulmonary biology/homeostasis, 96-98
  - in respiratory inflammation, 89-90, 96-98
  - in septic shock, 407-409
  - in signal transduction, 31
    - H7-sensitive kinases involved in, 33
    - Jak family tyrosine kinases in, 32-33
    - MAP kinases in, 33
    - protein kinases involved in, 31-34
    - second messenger(s) involved in, 34
    - src-family kinases in, 33-34
    - transcriptional factor(s) involved in, 34-35
    - tyrosine kinases in, 32-34
  - viral stimulation of, 93-98
- Interleukin-11 receptor, and gp130, 2, 16
- Interleukin-12 (IL-12), 2
  - actions of, 274
  - radioprotection by, 276-278
  - radiosensitization by, 276-278
- Interleukins. *See also* Inflammatory cytokines; Interleukin-6-type cytokines
  - pituitary hormones and, 429-431
- Ischemia
  - APP serum levels in, 493-495
  - IL-6 serum levels in, 493-495
- ISGF3. *See* Interferon-stimulated gene factor 3

**J**EBS. *See* Ets binding site  
 JRE-IL6. *See* Interleukin-6 response elements  
*junB* gene activation  
   H7-sensitive pathway in, 56–57  
   by IL-6, 56

**K**aposi's sarcoma cells, OSM and, 49

**L**eukemia inhibitory factor (LIF). *See also*  
   Inflammatory cytokines;  
   Interleukin-6-type cytokines  
   in APP induction, 15  
   in APRF phosphorylation, 23–24  
   cytokines related to, 37  
   and gp130, 1–2  
   and leukemic blast cell growth, 296–297  
   and leukemic cell lines, 295  
   in mammalian development regulation, 29  
   m-hLIF hybrids  
     amino acid sequences of, 166–167  
     binding activity of, 165–176  
     specific biological activity of, 168–169  
   mLIF binding activity, 168–169  
   mLIF crystal structure, 179–186  
   myeloproliferative disease models, 302  
   renal mesangial cells and, 424–425  
   in septic shock, 407–409  
 Leukemia inhibitory factor receptor  
   (LIF-R). *See also* Differentiation  
   stimulating factor/LIF receptor  
   gp130 in, 55  
   hLIF binding to, 165–166  
   and leukemic cell lines, 295–297  
   soluble subunits of, 213–215  
 Leukemia inhibitory factor response element  
   (LIF-RE)  
   activation of, 452–454  
   in myeloid leukemic cells, 452–454  
   and P19 carcinoma cell line, 426–428  
 Leukemic blast cell growth, IL-6-type  
   cytokines and, 295–297  
 Leukemic cell lines, IL-6-type cytokines and,  
   294–297  
 Lichen planus (LP), 432–433  
 LIF. *See* Leukemia inhibitory factor  
 LPS. *See* Bacterial endotoxin

**M**1. *See* Myeloid leukemic cell line  
 $\alpha_2$  Macroglobulin ( $\alpha_2$ M)  
   as hepatic acute phase gene inducer, 252  
   Stat proteins and, 58–59  
 $\alpha_2$  Macroglobulin ( $\alpha_2$ M) gene, IL-6 RE of,  
   253–255  
   protein binding at, 256–258  
   Stat factors and, 255–256  
 Macrophage growth factor (CSF-1), and  
   LPS resistance, 499–501

MAP kinases. *See* Mitogen-activated protein kinases  
 MDS. *See* Myelodysplastic syndromes  
 Melanoma  
   B-78/B-78 transfected cells  
     characterization of, 364–365  
     tumor growth of, 365–369  
   gene therapy of, 361–363  
   IL-6-type cytokines and, 362, 369–371  
 Mitogen-activated protein kinases (MAP kinases). *See also* Protein kinases;  
   Tyrosine kinase  
   activation of, 18, 33  
   IL-6 and, 18  
   in IL-11 signaling, 33, 37  
   in NF-IL6 phosphorylation, 18  
 Multiple myeloma. *See* Myeloma cell growth  
 Mycosis fungoides (MF), 432–433  
 Myelodysplastic syndromes (MDS), 294  
   IL-6 involvement in, 299–300  
 Myeloid leukemic cell line (M1)  
   LIF-RE activation in, 452–454  
   reconstituted IL-6 response in, 485–486  
 Myeloma cell growth  
   ATRA and, 457–458  
   IL-6 activity and, 131–133  
   inhibition of, 457–458  
 Myeloproliferative disease models, 294  
   IL-6/IL-11 excess, 301–302  
   LIF excess, 302

**N**BL. *See* Neuroblastoma  
 Neuroblastoma (NBL)  
   APP levels in, 443–444  
   metalloproteins, 443–444  
 NF-IL6  
   in APP gene regulation, 16–17  
   in C/EBP family, 16–17  
   in gene expression, 20  
   IL-6RE binding with, 17  
   macrophage-specific expression of, 17–18  
   NF-IL6  $\Delta$  mouse generation, 20  
   phosphorylation of, 18–19  
 NF- $\kappa$ B, 3  
   in gene expression, 20  
   as GR target, 81  
   steroid receptor antagonism with, 84  
   YY1 competition with, 245–249  
 N-ras genes  
   IL-6 and, 300  
   in MDS, 300

**O**ncostatin M (OSM). *See also*  
   Inflammatory cytokines;  
   Interleukin-6-type cytokines  
   APP induction by, 15, 47–48  
   in APRF phosphorylation, 23–24  
   blood clearance of, 43–45

- cytokines related to, 37, 42  
expression in AML, 299  
and gp130, 1-2, 42  
IL-6 induction by, 48  
and Kaposi's sarcoma cells, 49  
and leukemic cell lines, 295  
*n vivo* properties of, 42-49  
properties shared with other cytokines, 49  
in septic shock, 407-409  
therapeutic potential of, 49  
thrombocytopenia palliation by, 47  
thrombopoietic activity of, 45-46  
tissue distribution of, 43-45
- Oncostatin M (OSM) receptor  
gp130 in, 2, 55  
soluble subunits of, 213-215
- op/op* mice, LPS resistance in, 499-501
- OSM. *See* Oncostatin M
- Osteoporosis  
gonadotrophin levels and, 431  
IL-6 and, 212, 376-377  
in IL-6-deficient mice, 375-376  
inflammatory cytokines and, 430  
ovariectomy-induced, 375-377, 431
- Ovarian cancer, IL-6 serum levels in, 446-448
- P**53. *See also* Transcription factors  
C/EBP modulation by, 4-9  
and expression vectors, 6  
and hepatic IL-6 response, 4-10  
and IL-6 promoter activity, 5, 7, 9  
mutations in, 4-6  
and protein-protein interactions, 9-10  
proteins binding to, 4  
and reporter construct p50-2, 5-6  
as transcription regulatory factor, 4-10
- Palindromic interferon response element (pIRE). *See also*  $\gamma$ -IFN activated sequence  
IL-6 activation of, 349-352  
IL-6-dependent complexes with, 350-351  
sequences of, 349
- pIRE. *See* Palindromic interferon response element
- Pituitary hormones, and interleukin secretion, 429-431
- Preterm premature labor (PTL), amniotic IL-6 levels in, 10-12
- Protein kinases. *See also* H7-sensitive kinases;  
Mitogen-activated protein kinases;  
Tyrosine kinases  
in IL-11 signaling, 31-34
- Psoriasis, 432-433
- PTL. *See* Preterm premature labor
- R**A. *See* Retinoic acid  
*ras* gene, IL-6 expression and, 300
- Respiratory inflammation. *See also* Asthma  
IL-11 in, 89-90
- Respiratory viruses  
and asthma, 97  
and IL-11 production, 96
- Retinoic acid (RA). *See also* All-trans retinoic acid  
and APP synthesis, 419-421
- S**AA. *See* Serum amyloid A
- Septic shock  
IL-6-type cytokine levels in, 336, 407-409  
LPS in, 315, 336-338
- Serum amyloid A (SAA)  
IL-6 induction of, 102, 104-106  
inflammation levels of, 238  
mRNA half life, 105
- SIF. *See* Stat proteins
- Signal transduction. *See also* IL-6 signal transduction pathway  
gp130 in, 25-26  
H7-sensitive pathway in, 55-57  
IL-6 receptor in, 55, 64-67  
IL-11-mediated  
H7-sensitive kinases in, 33  
and MAP kinases activation, 33  
protein kinases involved in, 31-32  
JRE-IL6-mediated, 64-67  
Ras-independent, 55  
Stat factors in, 55  
tyrosine kinases in, 32-34, 262
- SOD. *See* Superoxide dismutase
- Soluble gp130, 207, 211  
and IL-6R-IL-6 complex, 212-213
- Soluble interleukin-6 receptor (IL-6R), 207, 224-226  
gp130, 211  
IL-6 complex with, 211-212  
IL-6R protein, 208-211  
and IL-6-soluble gp130 complex, 212-213
- Stat proteins  
activation of, 64-66  
APRE recognition by, 58-59  
cloned cDNA of, 60  
and cytokine receptor action, 196-203  
and GAS/pIRE genes expression, 349-350  
as IL-6-induced DNA binding factors, 58-59  
IL-6 RE binding of, 62, 459-461  
in IL-6 signal transduction, 55-56  
in IL-11 signaling, 31-37  
and  $\alpha_2$ M REs, 58-59  
phosphorylation of, 55-56, 62, 349-350  
as transcriptional factors, 34-35

Steroid receptors. *See also* Glucocorticoid receptors

and gene expression, 80, 82-84

NF- $\kappa$ B antagonism with, 84

and positive transcription factors, 80, 84-86

synergism/antagonism models, 84-86

transcription factors association with, 80

Superoxide dismutase (SOD), 416-418

**T**AT. *See* Tyrosine aminotransferase  
Taxol

acute phase cytokines induction by, 108, 112-114

and endotoxin-responsive gene expression, 114

Thrombocytopenia, OSM palliation of, 47

Thrombopoiesis, OSM activity and, 45-46

TIMP-1. *See* Tissue inhibitors of metalloproteinases

Tissue inhibitors of metalloproteinases (TIMP-1)

inflammatory cytokine induction of, 49

interleukin induction of, 462-464

TNF- $\alpha$ . *See* Tumor necrosis factor

Transcription activation/repression model, 248

Transcription factors. *See also* Acute phase response factors; C/EBP; CHOP-10; NF-IL6; NF- $\kappa$ B

CRU binding with, 241-249

as cytokine signal targets, 238-239

estrogens modulation of, 3

glucocorticoid modulation of, 3

in IL-6 induction, 3

p53 modulation of, 4-9

and steroid receptors, 80, 84-86  
superfamily of, 79

Transcription factors (IRF-1/IRF-2)

IL-6 induction of, 349-352

and IL-6 tumor cell effects, 347-348

Tumor necrosis factor (TNF- $\alpha$ )

in APP induction, 15

in endotoxin resistance, 499-501

and GCSB, 71, 73-76

inhibition of

antioxidants and, 331-338

clinical benefits of, 331

compounds active in, 331-332

Tyrosine aminotransferase (TAT), 416-418

Tyrosine kinases. *See also* Protein kinases;

Tyrosine phosphorylation

families of, 32-34, 64-65

gp130 activation of, 56

in IL-6R-mediated signals, 64-67

in IL-6 signal transduction, 55-56, 62-63

in IL-11 signaling, 32-34

in JRE-IL6-Stat protein complexes, 62

and signal transmission, 55, 64-67, 262

in Stat protein phosphorylation, 55-56

Tyrosine phosphorylation

of APRF, 23-24, 229-231

differences in, 37

of gp130, 23-24, 55, 231-233

IL-6 induction of, 55-56, 231-233

of IL-6 RE complexes, 62

IL-6-type cytokines induction of, 23-24

in IL-11 signaling, 31-37

of Stat proteins, 55-56, 62, 349-350

**Y**Y1. *See under* Cytokine response unit



# Index of Contributors<sup>a</sup>

- A**arden, L.A., 129-135  
 Abdul-Ahad, A., 359-360, 375-387  
 Adler, G., 388-389  
 Ahmed, A.A., 450-451  
 Akira, S., 15-28  
 Ali, N., 274-281  
 Allison, A.C., 331-341  
 Altamura, S., 136-151  
 Andrzejewska, R., 398-399  
 Ansari, A.A., 499-501
- B**aumann, H., 189-206, 308-318, 375-387, 413-415  
 Bellavia, D., 262-273  
 Bennett, F., 152-164  
 Bereta, J., 416-418  
 Bing, Z., 238-251  
 Biró, J., 71-78  
 Bläsius, R., 452-454  
 Boguslawska-Jaworska, J., 391-394  
 Borden, E. C., 359-360  
 Braciak, T., 282-293  
 Brakenhoff, J.P.J., 129-135, 400-402  
 Breitmeyer, J.B., 359-360  
 Brombacher, F., 308-318  
 Burchert, M., 395-397  
 Burris, H., 359-360  
 Burstein, S.A., 42-54
- C**abibbo, A., 136-151  
 Campos, S.P., 189-206  
 Cappelletti, M., 262-273  
 Chebath, J., 342-356  
 Chevalier, S., 407-409, 482-484  
 Chybicka, A., 391-394  
 Ciapponi, L., 136-151  
 Ciliberto, G., 136-151  
 Clark, R., 165-178  
 Clement, C., 482-484  
 Costantini, F., 262-273  
 Cullinan, E., 29-30  
 Czapryn, M., 152-164
- D**e Hon, F.D., 129-135, 400-402  
 Demartis, A., 136-151  
 Dembińska-Kieć, A., 395-397  
 Dittrich, E., 222-237, 410-412  
 Drechsler, D., 359-360  
 Dreier, B., 252-261  
 Drews, K., 398-399, 505-507, 508-509  
 Dube, J., 152-164  
 Dulak, J., 395-397  
 Dziatkowiak, A., 477-479
- E**hlers, M., 207-221, 400-402  
 Eichman, W., 388-389  
 Einarsson, O., 89-101  
 Eisenbach, L., 342-356  
 Elias, J.A., 89-101, 375-387  
 Erren, A., 222-237  
 Eugui, E.M., 331-341
- F**alus, A., 71-78  
 Fattori, E., 262-273  
 Feldman, M., 342-356  
 Fey, G.H., 252-261, 375-387, 452-454, 457-458, 502-504  
 Fourcin, M., 407-409  
 Freer, G., 308-318  
 Fritz, S., 252-261, 457-458  
 Fujitani, Y., 55-70
- G**radient, R.A., 403-406  
 Gadzinowski, J., xv  
 Galanos, C., 308-318  
 Galazka, A., 359-360  
 Garcia, D., 120-128  
 Gascan, H., 407-409, 482-484  
 Gauldie, J., 282-293  
 Gearing, D., 189-206  
 Geba, G.P., 89-101  
 Gerhartz, C., 222-237, 410-412  
 Goppelt-Strübe, M., 424-425  
 Gordon, M.S., 375-387  
 Gorny, A., 493-495  
 Gough, N.M., 165-178  
 Graeve, L., 222-237, 410-412, 462-464  
 Graham, F., 282-293  
 Grant, K., 152-164  
 Grey, L. M., 179-188  
 Grossberg, S.E., 359-360  
 Grötzinger, J., 207-221, 400-402  
 Gryska, K., 413-415  
 Guillet, C., 407-409  
 Gulino, A., 262-273  
 Gutierrez-Ramos, J.-C., 308-318  
 Guzdek, A., 108-119, 416-418, 419-421
- H**ammacher, A., 422-423, 471-473  
 Hanson, M.B., 42-54  
 Haran-Ghera, N., 342-356  
 Harroch, S., 342-356  
 Hartner, A., 424-425  
 Hawley, R.G., 294-307  
 Heath, J.K., 179-188  
 Heinrich, P.C., 222-237, 361-374, 375-387, 410-412

<sup>a</sup> Italic numbers indicate Roundtable Discussion.

- Hemmann, U., 222-237  
 Heumann, R., 488-490  
 Hiemke, C., 468-470  
 Hirano, T., 55-70  
 Hocke, G.M., 252-261, 424-425,  
 426-428, 452-454, 457-458,  
 502-504  
 Horn, F., 222-237, 375-387  
 Howlett, G.J., 471-473  
 Huang, J., 238-251

**I**noue, M., 15-28  
 Izbicki, T., 443-445

- J**awiczi, J., 477-479  
 Jaworski, W., 391-394  
 Jedrzejczak, P., 496-498, 505-507  
 Jiang, S.-L., 102-107  
 Jones, E.Y., 179-188  
 Jung, A., 455-456

- K**alinski, P., 499-501  
 Karabon, L., 435-438, 439-442  
 Kasprzak, M., 496-498  
 Katz, A., 342-356  
 Keever, C., 359-360  
 Kishimoto, T., 15-28  
 Klein, B., 482-484  
 Köhler, G., 308-318  
 Koj, A., xiii, 108-119, 375-387  
 Kojima, H., 55-70  
 Komorowski, J., 429-431  
 Kopf, M., 308-318, 375-387  
 Koskela, K., 457-458  
 Koziol, M., 432-434  
 Krasowska, D., 432-434  
 Ksiażek, A., 432-434  
 Kumaki, S., 189-206  
 Kurpisz, M., , 496-498  
 Kushner, I., 102-107

- L**aba, A., 439-442  
 Laciak, M., 413-415, 474-476  
 Lahm, A., 136-151  
 Lai, C.-F., 189-206  
 Landry, M.L., 89-101  
 Lange, A., 435-438, 439-442  
 Laskowska-Klita, T., 443-445  
 Layton, M.J., 165-178  
 Lazzaro, D., 262-273  
 Li, L., 238-251  
 Liao, W. S.-L., 238-251  
 Libing, C., 450-451  
 Liden, S., 450-451  
 Lipińska, L., 443-445  
 Ljungberg, A., 450-451

- Löchner, K., 252-261  
 Lottspeich, F., 252-261  
 Lozanski, G., 102-107  
 Lu, S.-Y., 238-251  
 Lütticken, C., 222-237

**M**ackiewicz, A., xiii, 308-318, 361-374,  
 398-399, 413-415, 474-476,  
 493-495, 508-509

- MacMaster, J.F., 42-54  
 Madry, R., 446-449  
 Majewski, W., 493-495  
 Margulies, L., 1-14  
 Markowska, J., 446-449  
 Marschalek, R., 252-261  
 Maruszynski, M., 455-456  
 Matern, S., 462-464  
 Matsuda, T., 55-70  
 Matsusaka, T., 15-28  
 May, L.T., 120-128  
 McCoy, J.M., 152-164  
 Metcalf, D., 165-178  
 Metinko, A., 89-101  
 Moniewska, A., 439-442  
 Morella, K.K., 189-206  
 Moritz, R.L., 471-473  
 Müllberg, J., 207-221, 400-402, 462-464  
 Müller, H., 468-470

- N**akae, K., 55-70  
 Nakajima, K., 55-70  
 Ndubuisi, M.I., 120-128  
 Neta, R., 274-281  
 Neva, M., 457-458  
 Nicola, N.A., 165-178  
 Nishio, Y., 15-28  
 Nordlind, K., 450-451  
 Novak, J., 361-374

**O**llikainen, H., 457-458  
 Otten, U., 403-406  
 Owczarek, C.M., 165-178

- P**an, H., 1-14  
 Panettieri, R.A., Jr., 89-101  
 Paonessa, G., 136-151  
 Patel, K., 120-128  
 Pawelec, M., 395-397  
 Pawlikowski, M., 429-431  
 Pawlowski, T., 361-374  
 Pellniemi, T.-T., 457-458  
 Perck, D., 443-445  
 Peskar, B.A., 395-397  
 Pickorz, R.P., 452-454, 485-487  
 Pierzchalski, P., 465-467  
 Pietrzak, A., 432-434

- Piowowska, W., 477-479  
 Plusa, T., 455-456  
 Pojda, Z., 455-456  
 Poli, V., 262-273, 375-387  
 Polus, M., 395-397  
 Pouplard, A., 407-409  
 Puk, E., 496-498  
 Pulkki, K., 457-458
- R**  
 Radwan, J., 477-479  
 Rákász, É., 71-78  
 Ramsay, A., 308-318  
 Ray, A., 79-88  
 Ray, P., 79-88  
 Rayanade, R., 1-14  
 Remes, K., 457-458  
 Revel, M., 342-356, 375-387  
 Richards, C.D., 282-293  
 Richter, K., 252-261  
 Rillema, J.R., 42-54  
 Ripperger, J., 252-261, 457-458, 502-504  
 Ritch, P.S., 359-360  
 Rivkin, S., 359-360  
 Robinson, R.C., 179-188  
 Robledo, O., 482-484  
 Roeb, E., 361-374, 462-464  
 Rokita, H., 465-467  
 Rose-John, S., 207-221, 462-464  
 Rouleau, K.A., 42-54  
 Rybakowski, J.K., 474-476
- S**  
 Salvati, A.L., 136-151  
 Samols, D., 102-107  
 Savino, R., 136-151  
 Schiller, J., 359-360  
 Schneider, K., 252-261, 502-504  
 Schneider-Mergener, J., 222-237  
 Scoble, H., 152-164  
 Screpanti, L., 262-273  
 Schgal, P.B., xiii, 1-14, 375-387  
 Sciler, W., 468-470  
 Sellitto, C., 262-273  
 Shoyab, M., 42-54  
 Siedlecki, A., 395-397  
 Siegel, M.D., 79-88  
 Simpson, R.J., 422-423, 471-473  
 Skrzypczak, J., 496-498, 505-507, 508-509  
 Slupianek, A., 413-415, 493-495  
 Służewska, A., 474-476  
 Sobieska, M., 474-476  
 Sookdeo, H., 152-164  
 Stadler, B.M., 477-479  
 Stalińska, K., 416-418, 465-467  
 Staniszewski, R., 493-495  
 Staunton, D., 179-188
- Stępien, H., 429-431  
 Sterzel, R.B., 424-425  
 Stewart, C.L., 29-30  
 Stiefel, S.M., 274-281  
 Stoyan, T., 410-412  
 Strużyna, J., 455-456  
 Stuart, D.I., 179-188  
 Swider, C., 439-442  
 Szczapa, J., 398-399  
 Szczekliak, A., 477-479  
 Szczepanski, M., 388-389  
 Szewierski, Z., 446-449  
 Szperl, M., 499-501  
 Szwech, P., 499-501  
 Szymanowski, K., 505-507, 508-509
- T**  
 Takeda, T., 55-70  
 Tanaka, T., 15-28  
 Targonska, I., 388-389  
 Tomeczko, J., 435-438  
 Tomida, M., 480-481  
 Toniatti, C., 136-151  
 Toruniowa, B., 432-434  
 Tristram, D., 89-101  
 Truitt, R.L., 359-360  
 Twardy, D.J., 189-206
- U**  
 Urbanowska, E., 499-501
- V**  
 Vaickus, L., 359-360  
 Van Dijk, W., 319-330  
 Von Hoff, D.D., 359-360
- W**  
 Wallace, P.M., 42-54, 375-387  
 Wang, L., 1-14  
 Wang, X.-J., 15-28  
 Wang, Y., 189-206  
 Ward, L.D., 422-423, 471-473  
 Weber, J.S., 357-358, 375-387  
 Wegenka, U., 222-237  
 Wei, S., 15-28  
 Weiergräber, O., 222-237  
 Weinstock, J., 422-423  
 Welliver, R., 89-101  
 Wijdenes, J., 482-484  
 Wiktor-Jedrzejczak, W., 499-501  
 Wiktorowicz, K., 446-449, 474-476  
 Witt, P.L., 359-360  
 Wiznerowicz, M., 361-374  
 Wollmer, A., 400-402  
 Wulf, P., 485-487
- X**  
 Xing, Z., 282-293
- Y**  
 Yamanaka, Y., 55-70  
 Yang, Y.-C., 31-41

Yin, T., 31-41

Yoshida, N., 15-28

**Z**<sub>ak</sub>, J., 398-399

Žak, L., 398-399

Žak, T., 505-507, 508-509

Zhang, D., 102-107

Zhang, D.-H., 79-88

Zhong, J., 488-490

Zhou, Z., 89-101

Ziegler, S.F., 189-206

Zieleniewski, W., 491-492

